REMARKS/ARGUMENTS

35 U.S.C. §103(a) Dunn (US 5,721,359) in view of Foster (US 5,736,151)

Claims 1-8, 12-13, and 16-17 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dunn (US 5,721,359) in view of Foster (US 5,736,151). In making this rejection the Examiner states that "Dunn teaches modifying the oil carrier by heat or irradiation in order to render it sterile, see column 8, lines 42-50." The Examiner further states that "Dunn teaches that the composition is sustained-release, see claim 9, column 19." Applicants respectfully disagree with both assertions.

In asserting that Dunn teaches modifying the oil carrier by heat or irradiation the Examiner cites column 8, lines 42-50. The passage in question reads:

> "Carriers and vehicles include vegetable oils, dimethylacetamide, dimethylformamide, ethyl lactate, ethyl carbonate, isopropyl myristate, ethanol, polyols, for example, glycerol, propylene glycol, liquid polyethylene glycol, and the like. Any solid preparations for subsequent extemporaneous preparation of sterile injectable preparations are sterilized, by exposure to heat, cobalt 60 irradiation, or by exposure to a sterilizing gas, for example, ethylene oxide."

The issue is whether the phrase "solid preparations" refers to solids in a carrier or simply solids. If the term "solid preparations" refers simply to solids, then the carrier is not present when these preparations are being irradiated or heated. Dunn discloses three methods for sterilizing the solid preparations, that is, heat, cobalt 60 irradiation, and exposure to ethylene oxide. As noted in Remington, The Science and Practice of Pharmacy (19th Edition p. 765), ethylene oxide is not generally used to sterilize liquids. Ethylene oxide is toxic, carcinogenic, teratogenic, and difficult to remove from the objects being sterilized. Products sterilized with ethylene oxide need to be quarantined for about fourteen days to eliminate the absorbed residues of ethylene oxide. As noted in the Matheson Tri-Gas MSDS for ethylene oxide, it is soluble in water and organic solvents. Thus, if ethylene oxide were used to sterilize a solid in one of the carriers described by Dunn, it would dissolve in the carrier and would not be readily removed. Ethylene oxide residues are not desirable in a pharmaceutical product. Applicants also note that in the passage above, Dunn refers to "solid preparations for subsequent extemporaneous preparation of

sterile injectable preparations..." Clearly, the term "solid preparations" does not refer to solids in a carrier because these preparations require further steps to produce "sterile injectable preparations." If a carrier were present, the preparations would be suitable for injection, and would not require further processing.

Applicants further respectfully submit that the term "solid preparations" refers to a dosage form. Dosage forms are discussed in Dunn (column 8 lines 14 to 20):

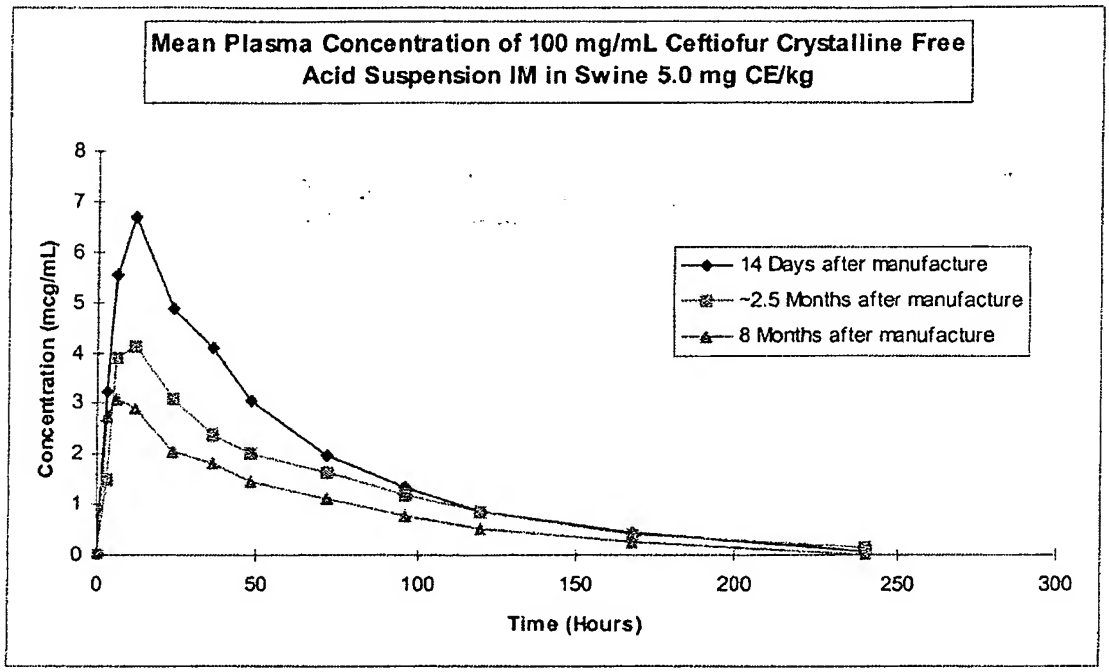
> Examples of suitable dosage unit forms in accordance with this invention are liquid preparations in suitable liquid vehicles for intramuscular, intramammary and intravenous administration, suppositories and sterile dry preparations for the extemporaneous preparation (mixing just prior to administration) of sterile injectable preparations in a suitable liquid vehicle or for administration as a solid implant.

Applicants respectfully submit that the person skilled in the art would conclude that in the passage in Dunn, quoted above, the term "solid preparations for subsequent extemporaneous preparation of sterile injectable preparations" (column 8 lines 47 to 48) refers to the dosage form described as "sterile dry preparations for subsequent extemporaneous preparation (mixing just prior to administration) of sterile injectable preparations" (Column 8 lines 17 to 19). Clearly this dosage form is a dry solid, and Applicants respectfully submit that the "solid preparations" (column 8 line 47) are dry solids. Since the carrier is not present when the solid preparations are being sterilized, the carrier is not subject to heat or irradiation. The Examiner has not refuted or even discussed Applicants' argument, but instead has merely repeated the assertion that "Dunn teaches modifying the oil carrier by heat or irradiation in order to render it sterile."

The Examiner has stated that Dunn teaches "that the composition is sustained-release." As Applicants have set forth before, the compositions of Dunn (US 5,721,359) do not provide sustained release performance of the compositions of the present invention. Specifically, the compositions of Dunn do not provide predictable sustained release of one or more bioactive agents upon administration immediately after manufacture of the composition and throughout their shelf life. A formulation containing 100 mg/ml crystalline ceftiofur free acid was prepared according to example 4 of Dunn. The formulation was administered intra-muscularly to swine at 14 days, approximately 2.5 months and 8 months after preparation at a dose of 5.0 mg of

ceftiofur equivalent (CE)/kg body weight. Although there were no noticeable changes in the formulation's potency, the release profile of the formulation changed noticeably over time. This is illustrated by the following graph.

In-vivo Drug Release Profile Changes Over Time for 100 mg/ml Crystalline Ceftiofur Free Acid Formulation of the Dunn Patent Administered IM in Swine



As Applicants have set forth, the compositions of Dunn are prepared by sterilizing a solid preparation. The compositions of Dunn do not involve a modified carrier as used in Applicants' invention. This argument is supported by the fact that the compositions of Dunn do not provide the same results as the compositions of Applicants' invention. Accordingly the compositions of Dunn are not similar to those of Applicants' invention. The addition of Foster to Dunn teaches coconut oil, but cannot overcome the problem that the formulations of Dunn are fundamentally different from those of Applicants' invention.

The confusion between Dunn and Applicants' invention appears to arise from the term "sustained-release." While the compositions of Dunn are said to be "sustained-release" they are

not sustained-release in the same sense as the compositions of Applicants' invention. In order to clarify this point Applicants respectfully provide the following analogy. Consider an issued patent for a bicycle tire and a patent application for a tire suitable for a drag racing vehicle. Both the patent and the application clearly relate to tires. However even if the bicycle is ridden under extremely favorable conditions, by highly skilled athletes, it will rarely go faster than 50 miles per hour. On the other hand, high performance drag racing vehicles will reach speeds well in excess of 300 miles per hour over the quarter mile drag strip. Clearly the bicycle tire is not the same as the tire of a drag racing vehicle. Merely because the bicycle tire and the drag racing tires are both tires does not mean that the bicycle tires render the drag racing tires obvious. Similarly, Applicants respectfully submit that the compositions of Dunn are not prepared in the same way as Applicants' compositions and do not have the properties of the compositions of Applicants' invention. Thus, Dunn in view of Foster does not render Applicants' invention obvious. Reconsideration of this rejection is respectfully solicited.

If the Examiner believes that personal communications will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favorable consideration of this application is respectfully requested.

Respectfully submitted,

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